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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,757	02/12/2001	Robert W. Mahley	6510096CIP3	9705

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,757	MAHLEY ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *5-18 and 23-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,19-22 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 27, 2004 has been entered.

This Office Action is a response to Applicant's request for continued examination (RCE) filed April 27, 2004, and amendment and response to the Final Office Action (mailed December 31, 2003), filed April 27, 2004 wherein claims 1-4 and 19-22 have been amended, and claim 29 is newly submitted.

Currently, claims 1-29 are pending in this application.

It is noted that Claims 5-18 and 23-28 are withdrawn from further consideration pursuant to 37 CFR 1 .142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made with traverse on September 11, 2002, recorded in the previous Office Action December 18, 2002.

Claims 1-4, 19-22, and 29 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 19-22, and 29 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the particular and specific compounds disclosed in the specification (see page 15 line 1-3 of the specification herein) employed in the claimed pharmaceutical composition herein, does not reasonably provide enablement for any substances or compounds represented by "an agent that binds specifically to apolipoprotein E4 (apoE4) and disnmts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" or "an agent that reduces apolipoprotein E4 (apoE4) domain interaction by at least about 10%, wherein said agent is an organic molecule having a molecular weight in a range of from about 50 daltons to about 2500 daltons, and wherein said agent inhibits formation of a salt bridge between Arg-61 and G1u-255 of apoE4", or "a blocked amino acid, a dye, a monosulfate, and a monosulfoalkyl compound" recited in the claims herein.

These recitations, "an agent that binds specifically to apolipoprotein E4 (apoE4) and disnmts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" or "an agent that reduces apolipoprotein E4 (apoE4) domain interaction by at least about 10%, wherein said agent is an organic molecule having a molecular weight in a range of from about 50 daltons to about 2500 daltons, and wherein said agent inhibits formation of a salt bridge between Arg-61 and G1u-255 of apoE4", are seen to be merely functional language.

Even regarding the recitation "a blocked amino acid, a dye, a monosulfate, and a monosulfoalkyl compound", one skilled in the art would clearly recognize that "a blocked amino acid, a dye, a monosulfate, and a monosulfoalkyl compound" would encompass widely various and numerous compounds which have separate and patentably distinct structures, possessing very different physical, chemical, biological and physiological properties or activities; moreover, they are classified in different subclasses of class 514.

Moreover, note that these recitations broadly encompass those known and unknown compounds as of the instant filing date, as well as those future known compounds yet to be discovered.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a pharmaceutical composition for the particular treatment.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad as discussed above.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997) at 1406: stating this usage does "little more than outline goal appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". The CAFC further clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "an agent that binds specifically to apolipoprotein E4 (apoE4) and disnmts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" or "an agent that reduces apolipoprotein E4 (apoE4) domain interaction by at least about 10%, wherein said agent is an organic molecule having a molecular weight in a range of from about 50 daltons to about 2500 daltons,

and wherein said agent inhibits formation of a salt bridge between Arg-61 and G1u-255 of apoE4", or "a blocked amino acid, a dye, a monosulfate, and a monosulfoalkyl compound", recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides several particular compounds for this kind of functional compounds for the composition (see page 15 line 1-3 of the specification herein).

Thus, Applicants functional language at the points of novelty fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph. Claims employing functional language at the exact point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).
The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, as

discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the pharmaceutical compositions herein.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a host (e.g., a human) any compounds represented by "an agent that binds specifically to apolipoprotein E4 (apoE4) and disnmts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" or "an agent that reduces apolipoprotein E4 (apoE4) domain interaction by at least about 10%, wherein said agent is an organic molecule having a molecular weight in a range of from about 50 daltons to about 2500 daltons, and wherein said agent inhibits formation of a salt bridge between Arg-61 and G1u-255 of apoE4", or "a blocked amino acid, a dye, a monosulfate, and a monosulfoalkyl compound".

See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur

with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added). In the instant case, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having claimed functional properties in the pharmaceutical compositions herein to be administered to a host. Thus, the teachings of the book clearly support that the instant claimed invention is highly unpredictable.

Further, these recitations broadly encompass those known and **unknown** compounds having the recited functions as of the instant filing date. Note those **future known** compounds yet to be discovered and/or made. Hence, those unknown or future known compounds encompassed by the claims herein must require to additional or future research to discover, make/synthesize, establish or verify their usefulness. Therefore, the skilled artisan has to exercise **undue experimentation** to practice the instant invention.

The presence or absence of working examples and the quantity of experimentation necessary:

As discussed above, only several particular compounds for this kind of functional compounds employed in the composition herein is disclosed in the specification. Moreover, it is noted in the specification that Applicant admits that

"In an initial screen, 14 compounds interfered with domain interaction and 6 partially interfered. In a follow-up assay, 8 of the 14 compounds were confirmed to interfere with domain interaction with little or no effect on the binding of apoE3 to the

emulsions. Table 9 shows the results of the eight compounds that interfere with domain interaction"

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims since the initially screening test for very limited specific compounds is not considered to sufficient enabling disclosure. Moreover, the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of the ingredients in the claimed composition. See MPEP § 716.02(d). As a result, necessitating one of skill to perform an exhaustive search for the embodiments of any known and unknown compounds having those functions encompassed in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all compounds encompassed in the instant claims employed in the claimed compositions to be administered to a host, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 19-22, and 29 are rejected under 35 U.S.C. 102(a) as being anticipated by Scolnick (WO 95/06470).

Scolnick discloses that a HMG-CoA reductase inhibitor, a statin such as lovastatin, simvastatin, pravastatin, and fluvastatin, being an agent that specially reduces apolipoportein E4, with a pharmaceutical acceptable excipient, is useful in a pharmaceutical composition administered to be or a pharmaceutical formulation. These statins are known to have molecular weight in a range within the instant claim. See page 3-4, and page 11-14, Example 1-2. In regard to the recitation "specifically reduces apolipoprotein E4 domain interaction by at least about 10%", the testing results of "% Change in Mean ApoE" at page 12 in Scolnick read on this recitation, more than 10%.

Note that Applicant admits regarding the prior art in the "BACKGROUND OF THE INVENTION" of the specification at page 3 line 29-30: "Recently, cholesterol lowering drugs, the statins, have been suggested for use in treating Alzheimer's disease by lowering apoE4 levels. WO 95/06470."

Scolnick also discloses the compound of formula (I) when Z is (b), (c), (d), (e), or (f) (see page 6 line 13 to page 7 line 25) is deemed to a dye, since these Z groups in the compounds are chromophore groups; thus these compounds of Scolnick are coloring substances. Thus, the limitation in claim 29 is deemed to be met.

Thus, Scolnick clearly anticipates the claimed invention herein.

Moreover, Applicant is requested to note that it is well settled that "intended use" or inherent property of a composition or product, e.g., "specifically reduces apolipoprotein E4 domain interaction by at least about 10%" in the instant claims, will not further limit claims drawn to a composition or product. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Applicant's remarks filed April 27, 2004 with respect to this rejection of claims 1-4 and 19-22 made under 35 U.S.C. 102(a) in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art. These remarks are believed to be adequately addressed by the rejection presented above.

Additionally, Applicant argues that the recitation of "specifically reduces apolipoprotein E4 domain interaction by at least about 10%" in the instant claims is not taught in Scolnick. However, as discussed above, the recitation is clearly disclosed in Scolnick.

Further, any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product.

Thus, Scolnick clearly anticipates the claimed invention herein.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
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August 18, 2004